

The claims in the pending application are generally directed to nitrosated and/or nitrosylated prostaglandin compounds, compositions and kits comprising nitrosated and/or nitrosylated prostaglandin compounds, and, optionally, other compounds, and the methods of use for the compounds and/or compositions.

II. The Restriction Requirement is Improper

Applicants respectfully submit that the Restriction Requirement is improper. The Patent Office has issued numerous office actions over the past 4+ years of prosecution in which all the pending claims were examined together. For the Examiner's convenience a listing of the Office Actions issued to date is given below:

1. Restriction Requirement dated May 8, 2001
2. Office Action dated July 24, 2001
3. Final Office Action dated January 22, 2002
4. Petition from Restriction Requirement Decision dated October 18, 2002,
granting Applicant's Petition
5. Office Communication dated February 21, 2003, withdrawing the finality of the Office Action dated January 22, 2002.
6. Office Communication dated August 29, 2003
7. Office Action dated November 25, 2003
8. Office Communication dated May 19, 2004

In the final Office Action dated January 22, 2002, the Examiner allowed claims 2-8, 10-17, 19-31, 33-40 and 104-106 to the extent that they read on the elected species, i.e., the nitrosated prostaglandins (i.e., prostaglandins that contain at least one -NO₂ group). *See* Office Action dated January 22, 2002, at Paragraph No. 1. The Examiner objected to the claims as being directed to a misjoinder of inventions of nitro (nitrosated prostaglandins, i.e., prostaglandins that contain at least one -NO₂ group) and nitroso (nitrosylated prostaglandins, i.e., prostaglandins that contain at least one -NO group)). *See* Office Action dated January 22, 2002, at Paragraph No. 2.

Applicants then filed a petition dated April 18, 2002, requesting reconsideration and reversal of the Examiner's decision on the issue of misjoinder. On October 18, 2002, Applicants'

Petition was **granted in full** and the application was forwarded to the Examiner for consideration to the Applicant's response filed July 22, 2002.

Pending claims 2-8, 10-17, 19-31, 33-40, 104 -106 and 116 (same as cancelled claim 1) are essentially the **same claims** that were pending at the time Applicant's Petition was **granted in full**.

III. Proposed restriction requirement

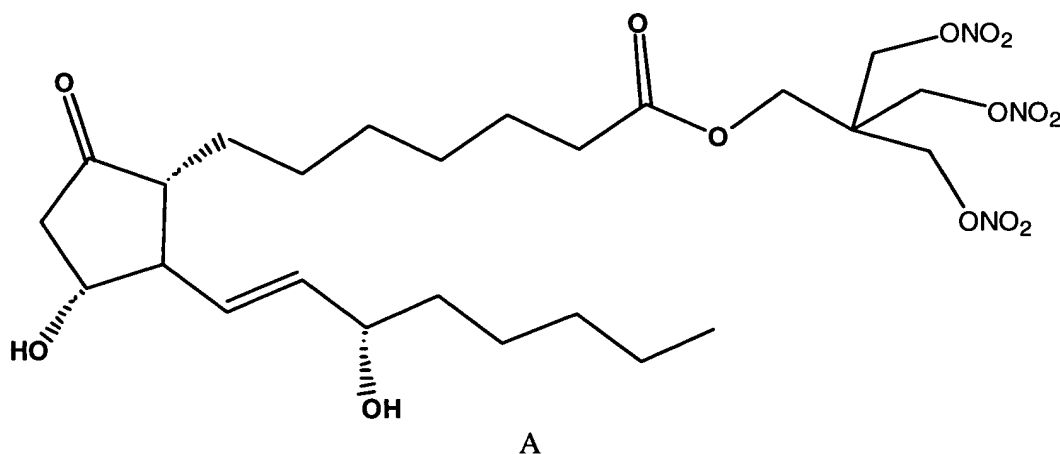
In view of the above, Applicant's respectfully submit that the Restriction Requirement is improper and request that it be withdrawn. Applicants respectfully propose that all the claims be examined together.

IV. Provisional Response to Restriction Requirement

Applicants provisionally elect Group II, claims 2, 3 and 116 drawn to the compounds of Formula I, with traverse.

V. Election of Species

In response to the election of species requirement for a compound, Applicants provisionally elect the nitrated prostaglandin of Formula A as the compound of Formula I, with traverse. The nitrated prostaglandin of Formula A, has the following structure:



The synthesis of this compound is described in Example 11 of the specification at page 52, line 6 to page 54, line 7.

The nitrated prostaglandin of Formula A is the **same species** as the Applicant elected in the response filed on **June 8, 2001**, over three years ago. The Examiner searched the nitrated prostaglandin of Formula A and found the claims to be allowable. See Office Action dated

January 22, 2002, at Paragraph No. 2. Again, the pending claims are essentially the same claims the Examiner previously found to be allowable over the prior art.

VI. Four Year Prosecution History

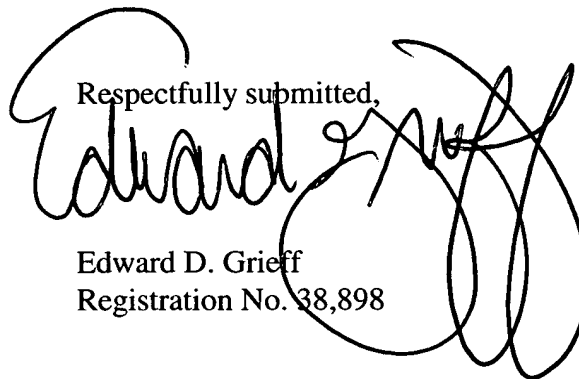
The U.S. Patent Office has already conducted prior art searches for the pending claims. In the Office Action dated January 22, 2002, the Examiner allowed claims 2-8, 10-17, 19-31, 33-40 and 104-106 to the extent that they read on the elected species, i.e., the nitrosated prostaglandins. Applicant's Supplemental Response and Amendment dated June 3, 2004, addressed the Examiner's rejection raised in the Office Action dated November 25, 2003. In view thereof, Applicants respectfully submit that the claims are in condition for allowance.

Applicants further note that in the corresponding PCT application (PCT/US00/05286), the Notification of Transmittal of International Preliminary Examination Report (attached hereto as Exhibit A) does not set forth any lack of unity objection, and indicates that claims 1-115 are allowable because the prior art does not teach or fairly suggest the compounds and their properties.

VII. Conclusion

Applicants respectfully request that the restriction requirement be withdrawn, as the 4+ years of prosecution in this application has shown that the pending claims are in condition for allowance.

Respectfully submitted,

A large, stylized handwritten signature in black ink, appearing to read 'Edward D. Grieff', is written over the typed name and registration number.

Edward D. Grieff
Registration No. 38,898

Date: October 15, 2004
WILMER CUTLER PICKERING
HALE AND DORR LLP
1455 Pennsylvania Avenue, NW
Washington, DC 20004
Phone: (202) 942-8453

Exhibit A

PATENT COOPERATION TREATY

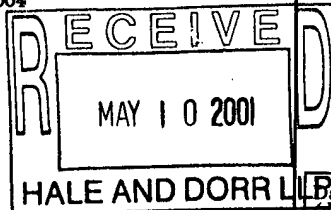
From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: EDWARD D. GRIEFF
HALE AND DORR LLP
1455 PENNSYLVANIA AVENUE, NW
WASHINGTON DC 20004

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)



Date of Mailing
(day/month/year)

08 MAY 2001

Applicant's or agent's file reference

102258.350

IMPORTANT NOTIFICATION

International application No.

PCT/US00/05286

International filing date (day/month/year)

01 MARCH 2000

Priority Date (day/month/year)

01 MARCH 1999

Applicant

NITROMED, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks
Box POT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

ROBERT GERSTL

Telephone No. (703) 308-1235

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 109258.350	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/410)	
International application No. PCT/US00/05286	International filing date (day/month/year) 01 MARCH 2000	Priority date (day/month/year) 01 MARCH 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C07C 405/00; A61K 31/557 and US Cl.: 560/121; 562/503; 514/530, 573		
Applicant NITROMED, INC.		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of <u>14</u> sheets. <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of <u>1</u> sheets.
3.	This report contains indications relating to the following items: <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 12 SEPTEMBER 2000	Date of completion of this report 19 APRIL 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer ROBERT GERSTL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/05286

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed☒ the description:

pages (See Attached)

, as originally filed

pages , filed with the demand

pages , filed with the letter of

☒ the claims:

pages (See Attached)

, as originally filed

pages , as amended (together with any statement) under Article 19

pages , filed with the demand

pages , filed with the letter of

☒ the drawings:

pages (See Attached)

, as originally filed

pages , filed with the demand

pages , filed with the letter of

☒ the sequence listing part of the description:

pages (See Attached)

, as originally filed

pages , filed with the demand

pages , filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig. NONE5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/05286

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)

Claims 1-115

YES

Claims NONE

NO

Inventive Step (IS)

Claims 1-115

YES

Claims NONE

NO

Industrial Applicability (IA)

Claims 1-115

YES

Claims NONE

NO

2. citations and explanations (Rule 70.7)

Claims 1-115 the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the compounds and their properties.

_____ NEW CITATIONS _____

NONE

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-62, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) 64-77, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Page 63, filed with the letter of 13 February 2001.

This report has been drawn on the basis of the drawings,
page(s) 1-4, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE